I. REMARKS

A. Status of the Claims

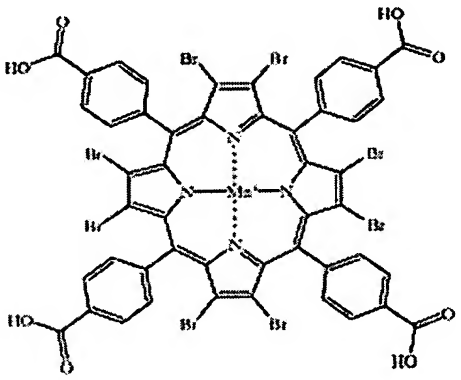
Claims 1-3 were originally filed with the case. Claims 1-3 were rejected in an Official Action, mailed on November 17, 2004. Claims 1 and 3 were amended and claims 4-7 were added in a Response to Office Action filed on May 17, 2005. All claims are rejected in the outstanding Official Action. No claims are amended, added, or canceled herein. Therefore, claims 1-7 remain pending.

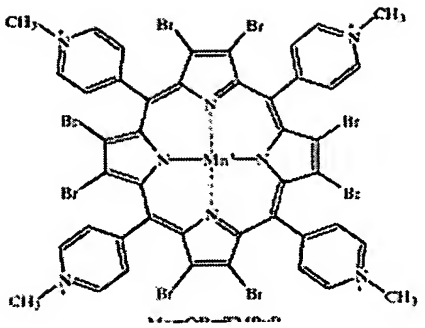
B. The Claims are Patentable Over Malfroy-Camine, LaHaye, Campbell and Crapo

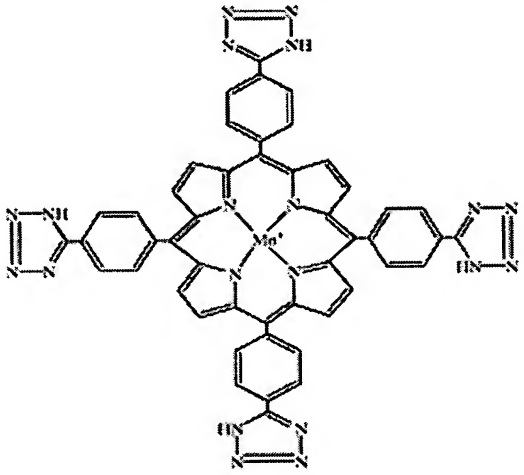
In the previous Office Action, claims 1-3 were rejected as being unpatentable over Malfroy-Camine (U.S. Patent No. 6,046,188) and LaHaye (U.S. Patent No. 5,075,116). Malfroy-Camine was said to teach the use of the claimed compounds as antioxidants for the treatment of diseases by acting as a free radical scavenger. The previous Action acknowledged that Malfroy-Camine lacks a teaching the treatment of macular degeneration, diabetic retinopathy or retinal edema. LaHaye was said to teach the use of free radical scavengers and antioxidants for treating diseases such as macular degeneration. Thus, the previous Action took the position that it would have been obvious to the skilled artisan to use the claimed compounds for the treatment of macular degeneration. In the present Action, all claims are rejected as being unpatentable over Malfroy-Camine and LaHaye for the reasons stated in the previous Action. In the present Action, Campbell and Crapo are added to the obviousness rejection, but it is not clear whether the addition of these references is meant to supplement the previous rejection or to comprise a new and separate rejection. Campbell is said to teach the use of the claimed compounds in a pharmaceutical formulation which can be

administered by any appropriate route of administration, such as injection. The Action acknowledges that Campbell lacks a teaching of the use of the compounds described to treat ocular disorders such as macular degeneration. Crapo is said to teach that compounds with a porphyrin ring, which are said to be SOD mimetics, can be used to treat disorders such a glaucoma and macular degeneration. Applicants respectfully traverse.

The present invention is directed to the use of superoxide dismutase mimics, which are large, complex molecules that are complexed with manganese, administered to the eye topically or parenterally, or by ocular injection, to treat AMD, DR, and/or retinal edema. The compounds for use in the methods of the invention include a manganese complexed with two nitrogens, two oxygens and an ion. The complex includes a ring structure comprising two six-membered aromatic rings, substituted with a number of possible substituents, defined in the claims. The compounds for use in the present invention are quite different from those compounds described in Crapo and Campbell. The compounds described in Crapo include a manganese complexed to four nitrogens, each of which is one member of a five-membered ring and the four, five-membered rings are attached to each other via a carbon between them, with each carbon containing a string of R substituents. For example, the compounds described in Crapo include the following:

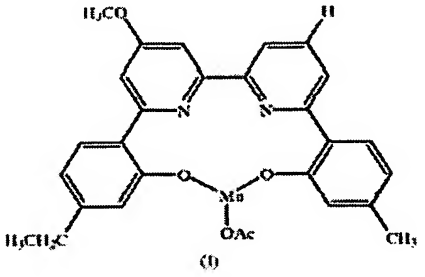






and

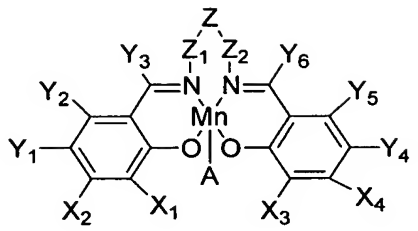
As shown above, the compounds described in Crapo are much larger than those used in the methods of the present invention. One of the objects of the present invention is to provide lower molecular weight compounds that catalyze superoxide disproportionation with efficiency comparable to endogenous Mn SOD, while avoiding the bioavailability and immunogenic issues thought to be due to the higher molecular weight species (Spec. page 7, lines 18-24). Furthermore, the compounds described in the Campbell reference cited in the Action are quite different from those used in the methods of the present invention, as can be seen in the formula I, which represents the compounds described in Campbell:



In light of the differences in the compounds described in the references cited, and the fact that neither reference discusses the use of the compounds described for treatment of AMD, diabetic retinopathy, or retinal edema, it is submitted that the cited references cannot render the claimed invention obvious.

As stated previously, LaHaye discusses the use of a composition of antioxidant vitamins, in the form of a caplet or tablet to be taken orally, to treat macular degeneration. LaHaye does not discuss other antioxidant compounds, nor does it discuss other routes of administration. There is no suggestion within LaHaye to use anything other than antioxidant vitamins in a caplet or tablet, with minerals, to treat ocular disorders. Malfroy-Camine, on the other hand, discusses only the use of antioxidant salen-transition metal complexes for the treatment of free radical-associated diseases. LaHaye contains no suggestion that antioxidant compounds complexed with transition metals could be administered topically or parenterally to the eye or by ocular injection. The minerals included in the compositions disclosed in LaHaye are not complexed with the antioxidant vitamins.

The present invention provides methods for treating AMD, DR, and/or retinal edema by administering to a patient a pharmaceutically effective amount of a compound of formula I:



I

It is submitted that the Action has taken the teaching of the present application and combined it with the disclosure in Campbell or Crapo that certain different and larger compounds are SOD mimetics or oxidant scavengers and may be useful to treat a variety of disorders other than AMD, DR or retinal edema, to state that it would have been obvious for one skilled in the art to treat these disorders with the smaller compounds of the present invention. This amounts to an improper "hindsight reconstruction" of the invention based upon the teaching in the present application. *See In re Fine*, 5 U.S.P.Q.2d 1596 (Fed. Cir. 1988). In *Fine*, the court explained that

> [t]o imbue one of ordinary skill in the art with knowledge of the invention in suit, when no prior art reference or references of record convey or suggest that knowledge, is to fall victim to the insidious effect of a hindsight syndrome wherein that which only the inventor taught is used against its teacher.

Fine, 5 U.S.P.Q.2d at 1600 (quoting *W.L. Gore & Assoc. v. Garlock, Inc.*, 721 F.2d 1540, 1553, 220 U.S.P.Q. 303, 312-13 (Fed. Cir. 1983)).

The rejection under § 103 based on the combination of Mayfroy-Camine, LaHaye, Campbell and Crapo amounts to a "picking and choosing" of certain parts of the references while ignoring other aspects of it. The Federal Circuit has held that "it is impermissible within the framework of 35 U.S.C. § 103 to pick and choose from any one reference only so much of it as will support a given position to the exclusion of other parts necessary to the full appreciation

of what such reference *fairly suggests* to one skilled in the art." *Bausch & Lomb, Inc. v. Barnes-Hind/Hydrocurve, Inc.*, 230 U.S.P.Q. 416, 419 (Fed. Cir. 1986) (quoting *In re Wesslau*, 353 F.2d 238, 241, 147 U.S.P.Q. 391, 393 (CCPA 1965)). What the Action ignores is the fact that nowhere within any of the cited references is a method for treating AMD, DR, and/or retinal edema via administration of the described compounds taught or suggested.

In light of the foregoing arguments, Applicants respectfully request that the obviousness rejection be withdrawn.

C. Conclusion

This is submitted to be a complete response to the outstanding Action. Based on the foregoing arguments, the claims are believed to be in condition for allowance; a notice of allowability is therefore respectfully requested.

The Examiner is invited to contact the undersigned attorney at (817) 551-4321 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

Teresa J. Schultz
Reg. No. 40.526
Attorney for Applicants

ALCON RESEARCH, LTD.
6201 S. Freeway, Q-148
Fort Worth, TX 76134-2099
(817) 551-4321

Date: 29 NOV. 2005